1-21-2019

Investigating the Role of Coil Designs and Anatomical Variations in Cerebellar TMS

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Abstract

Transcranial magnetic stimulation (TMS) is a non-invasive neuromodulation technique that is used for treating various neurological disorders such as major depressive disorder. TMS has been gaining popularity in the field of neurostimulation of the cerebellum, since the cerebellum is a complex structure connected with almost the entire central nervous system and TMS has promise for non-invasively probing cerebellar function. Recent studies have discovered that the cerebellum plays an important role not only in motor planning and behavior but also in the cognitive domain. However, few studies have explored how different coil designs and anatomical variations affect the effectiveness of cerebellar TMS. Therefore, in this paper, we investigated the effects of cerebellar TMS with different coil designs positioning on several locations. Finite-element modeling was conducted with Figure-8 coil and D-B80 coil. Each coil was positioned in the center, 1 and 3 cm to the left of center of the cerebellum, and all the locations were tangential to the scalp at a distance of 5 mm. Furthermore, 50 MRI derived head models were used in the computer modeling to examine how anatomical variations affect the distribution and intensity of electric field in cerebellar TMS.

Keywords

Anatomical variations, Cerebellar TMS, Coil Design

Disciplines

Bioelectrical and Neuroengineering | Biomedical Devices and Instrumentation | Electromagnetics and Photonics

Comments

This is a manuscript of an article published as Zhong, Xiaojing, Priyam Rastogi, Yifei Wang, Erik G. Lee, and David C. Jiles. "Investigating the Role of Coil Designs and Anatomical Variations in Cerebellar TMS." *IEEE Transactions on Magnetics* (2019). DOI: 10.1109/TMAG.2018.2890069. Posted with permission.

Investigating the role of coil designs and anatomical variations in cerebellar TMS

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Transcranial magnetic stimulation (TMS) is a non-invasive neuromodulation technique that is used for treating various neurological disorders such as major depressive disorder. TMS has been gaining popularity in the field of neurostimulation of cerebellum, since the cerebellum is a complex structure connected with almost the entire central nervous system and TMS has promise for non-invasively probing cerebellar function. Recent studies have discovered that the cerebellum plays an important role not only in motor planning and behavior but also in the cognitive domain. However, few studies have explored how different coil designs and anatomical variations affect the effectiveness of cerebellar TMS. Therefore, in this work we investigated the effects of cerebellar TMS with different coil designs positioning on several locations. Finite element modeling was conducted with Figure-of-8 coil and D-B80 coil. Each coil was positioned in the center, 1 cm and 3 cm to the left of center of the cerebellum and all the locations were tangential to the scalp at a distance of 5 mm. Furthermore, 50 MRI derived head models were used in the computer modelling to examine how anatomical variations affect the distribution and intensity of electric field in cerebellar TMS.

***Key Words*—Anatomical variations, Cerebellar TMS, Coil Design.**

I. Introduction

TRANSCRANIAL MAGNETIC STIMULATION(TMS) is a non-invasive neuromodulation technique which is capable of activating neurons in the brain. In TMS, a time-varying magnetic field generated by stimulator induces an electric field and causes depolarization of neurons in the targeted area via a stimulation coil [1]. When stimulation is applied repetitively over the course of weeks, the effects can create lasting changes to brain activity. US Food and Drug Administration (FDA) has approved TMS as a treatment for major depressive disorder in 2008 and for obsessive compulsive disorder (OCD) in 2018.

In the past several years, the cerebellum has also become a common target for TMS studies. The cerebellum is a multi-functional complex structure connected with almost the entire central nervous system [1]. Recent studies have discovered that the cerebellum plays an important role not only in motor planning and behavior but also in the cognitive domain [2]. And it has been reported that cerebellar TMS can influence motor system, memory and perception of time [1].

One challenge with using TMS is that it is often difficult to determine the spatial distribution of brain regions receiving stimulation, especially for cerebellum because of its unique shape and location. This is also due to individual anatomical differences and differences in the electromagnetic fields of different TMS coils. In addition, the depth of the cerebellum limits efficiency of magnetic stimulations [3] as the induce electric field reaches its maximum close to the surface of coil and then decays rapidly. The shape and size of TMS coils significantly affect the intensity and focality of stimulation, and in turn the response to stimulation. In addition, for cerebellar TMS, because the position on the brain and the anatomy of the cerebellum is so different than the motor cortex, studies commonly deliver stimulation at a fixed stimulator output for all subjects [3][4], the variability of stimulations between subjects is of interest. Some previous studies have compared the effects of different coil geometries on cerebellar TMS [3], while few studies have reported how anatomical variations play a part in affecting the distribution and intensity of induced electric field on cerebellum [5].

Therefore, in this paper, we compared the maximum electric fields induced in cerebellum for 50 MRI derived head models between two types of coils. The first coil is the Magstim 70 mm Figure-8 coil which is commonly used in TMS studies that prioritize stimulation focality, and the second coil is the MagVenture D-B80 butterfly coil which is commonly used in studies that prioritize greater depth of stimulation. Both coil were placed at three different locations to figure out how position affect stimulated area and induced electric field intensity in cerebellum.

II. Method

The 50 head models used in this study were developed by Lee et al. using the SimNIBS pipeline [6][7], which is used to segment anatomical regions from Human Connectome Project MRI images [8][9][10]. These models were created from healthy adults between the age of 22 to 35, with equal number of males and females. Seven different segmented anatomies including cerebellum, cerebrospinal fluid (CSF), grey matter (GM), skin, skull, ventricles and white matter (WM) constitute these models.

Finite element modeling of TMS coils and calculation of electric fields were conducted using Sim4life[11]. The simulations in this study were carried out with 1 mm isotropic voxels, and the total numbers of voxels are at the order of magnitude of six. The current applied to the TMS coils was 5000A peak to peak at a frequency of 2.5 kHz, which is comparable in intensity to a common value of a stimulator's maximum output [12]. The corresponding relative permittivity and electrical conductivity values for head models were taken from IT'IS Database [13]. A quasi-static, low frequency solver

Funded by ISU-UI Parnership Seed Grant Program – Iowa Brain Stim Collaboration

was used to calculate induced electric field in cerebellum. A Magstim 70 mm Figure-8 coil and a MagVenture D-B80 butterfly coil were used to compare how different coil geometries affect the stimulation on cerebellum. Magstim Figure-8 coil is a double 70 mm flat coil [14], and MagVenture D-B80 is a double 95 mm coil with an angle of 120° [15]. Results from Sim4life were exported to MATLAB for data analysis and interpretation.

As the stimulated area may differ and the induced electric field strength may alter with different coil positions, each coil was placed at the center, 1cm to the left and 3 cm to the left with respect to the vermis of the cerebellum, tangential to the scalp at a distance of 5 mm. The distance of 5mm is considered as the insulation thickness around coils. When we placed the coils, we kept the distance between the surface of each coil and the scalp as 5 mm. As a result, the distance from the center of Figure-8 coil to scalp is 5 mm as it is a flat coil, while the distance from the center of D-B80 coil to scalp is larger than 5 mm given the angle between two windings. Fig.1 has illustrated the distance of 5 mm from the surface of each coil to the scalp.

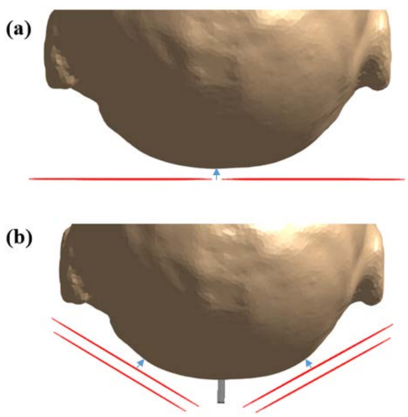

Fig. 1. Distance of 5 mm from the surface of (a) Figure-8 coil and (b) DB-80 coil to the scalp

Fig.2 has shown the positions of Figure-8 coil and D-B80 coil used in the simulations. For the six combinations of coil type and position, simulations on 50 MRI derived head models were conducted to examine how anatomical variations affect the electric field distribution of cerebellar TMS.

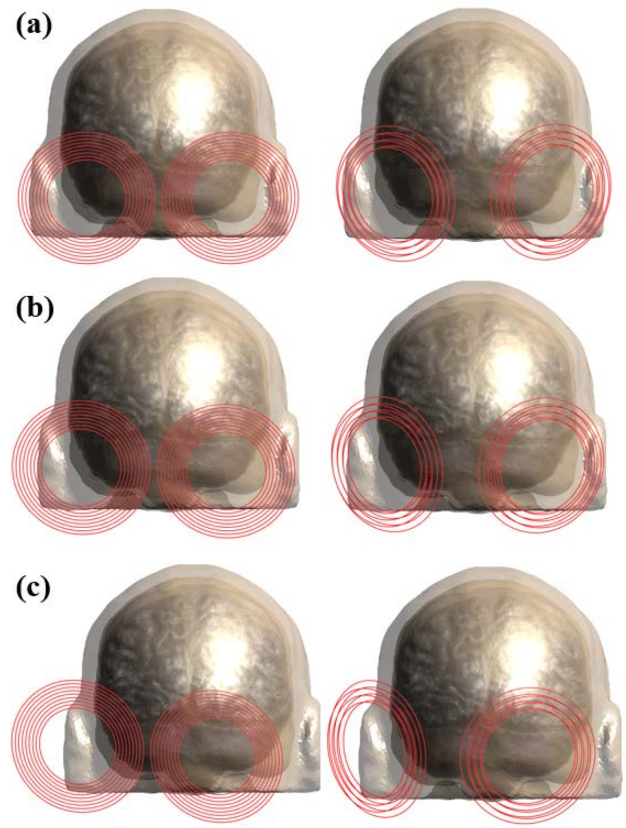

Fig. 2. Figure-8 coil (left) and D-B80 coil (right) (a) at the center (b) 1cm to the left (c) 3 cm to the left with respect to the center of cerebellum

To illustrate and compare the results of each set of simulations, two metrics, E-Max (the maximum E-field intensity in the cerebellum, we used mean value from the voxels with the largest 100 values) and V-Half (the volume of the cerebellum exposed to E-field intensities at least half E-Max), were employed[16].

III. Result

The results in this paper show how coil geometry and anatomical variation affect cerebellar stimulation.

The distributions of induced electric fields on cerebellum from the Figure-8 coil and D-B80 coil placed at different positions are shown in Fig.3. This is an example from one of the 50 MRI derived head models.

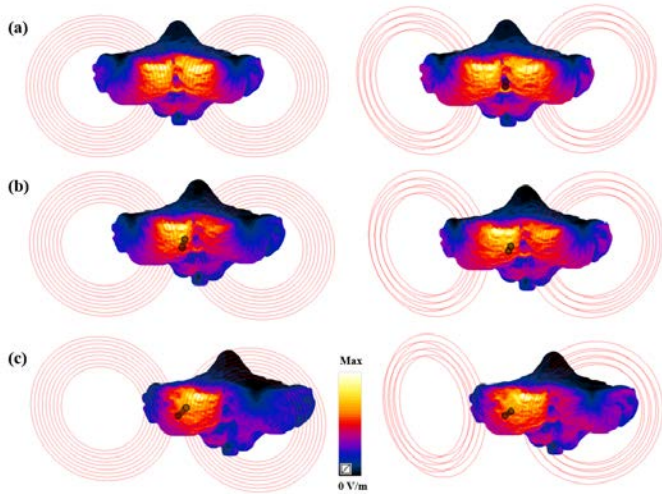

Fig. 3. Distribution of induced electric field on cerebellum when placing Figure-8 coil (left) and D-B80 coil (right) (a) at the center (b) 1cm to the left (c) 3 cm to the left with respect to the center of cerebellum

In this paper, the maximum electric field intensity (E-Max) and the volume of the cerebellum exposed to E-field intensities at least half E-Max (V-Half) were compared between the same coil at different positions, and between different coils at the same position. All the data points were included in the analysis and shown in Fig. 4 to Fig. 9. For each boxplot, the line that divides the box represents the median and the middle "box" represents the middle 50% of the values. The lower and upper borders of the box correspond to lower and upper quartile and the range from lower to upper quartile refers to the interquartile range. The points in boxplots are outliers if they are 1.5 times the interquartile range above the upper quartile or below the lower quartile. They are outliers in the boxplots but not in our experiments, so no data point has been removed when reporting the five number summaries.

A. *Figure-8 Coil*

For Figure-8 coil, the boxplots in Fig.4 illustrates the data of the stimulations with Figure-8 coil for each position from computational simulations. We can see some differences between three groups (Center group, L1cm group and L3cm group corresponding to the position with respect to the center of cerebellum). When analyzing the data, no parametric properties were assumed. Therefore, non-parametric Wilcoxon signed-rank test was used to check if there exists statistically significant difference of E-Max averaging over 50 head models between groups. Table I reports the p-value and a 95% confidence interval for each test.

TABLE I
TEST RESULTS OF DIFFERENCE BETWEEN POSITIONS FOR FIGURE-8 COIL

Figure-8 Coil	P-value	95% Confidence Interval
L1cm vs Center	< 0.0001*	(4.422, 8.418)
L3cm vs Center	< 0.0001*	(9.316, 15.272)
L3cm vs L1cm	< 0.0001*	(3.732, 7.980)

*statistically significant

It can be seen from the results that average E-Max values of L1cm and L3cm groups are significantly greater than that of Center group. In the meanwhile, the average E-Max values of L3cm group is significantly greater than that of L1cm group. The confidence interval measures the effect size by how much the position affect the electric field intensity.

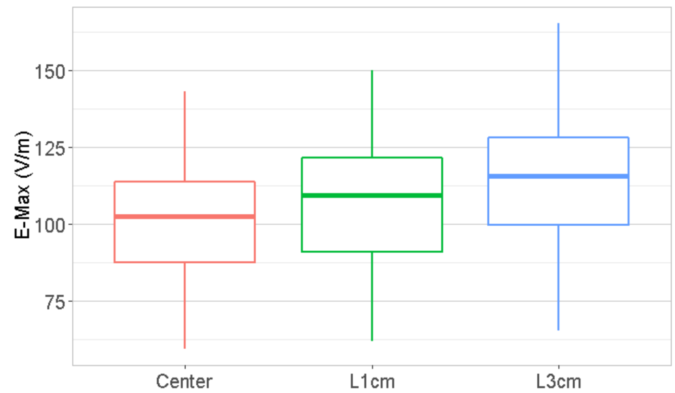

Fig. 4. Comparison of E-Max (V/m) between different positions of Figure-8 coil

Five number summaries of E-Max for 50 head models are given in Table II. The ranges of E-Max across 50 head models for all three groups are large due to anatomical variations, which highlights the importance of conducting simulations on a large amount of head models.

TABLE II
FIVE NUMBER SUMMARY OF E-MAX (V/M) FOR FIGURE-8 COIL

	Minimum	1st Quartile	Median	3rd Quartile	Maximum
Center	59.40	87.67	102.62	113.88	143.28
L1cm	61.95	90.89	109.58	121.65	150.25
L3cm	65.32	99.70	115.62	128.25	165.53

V-Half represents the volume of the cerebellum exposed to E-field intensities at least half E-Max, which is another very important metric to examine stimulation effects. From Fig.5, we can see that for Figure-8 coil, when moving the coil from the center of cerebellum to the left, there is no obvious trend of V-Half values as what we have seen in E-Max, and no significant changes can be seen. It means that E-Max increases as the coil position changing from center to the left without sacrificing the stimulated volume in cerebellum.

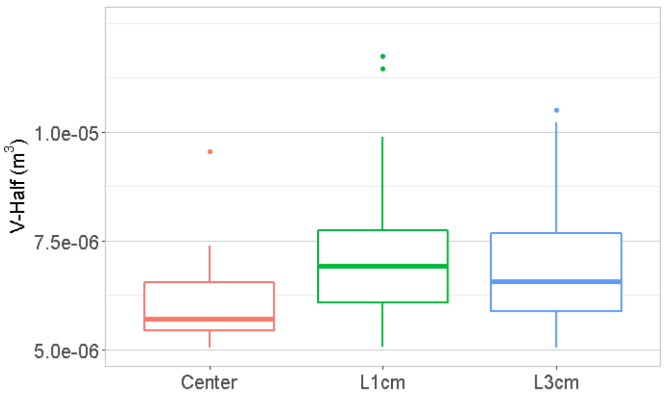

Fig. 5. Comparison of V-Half (m^3) between different positions of Figure-8 coil

B. *D-B80 Coil*

D-B80 butterfly coil has a different geometry than Figure-8 coil due to the angle between two windings. The same analysis procedure was conducted to the simulation results with D-B80 coil.

The boxplots in Fig.6 shows the maximum electric field intensity in cerebellum induced by D-B80 coil for all 50 head models at each position.

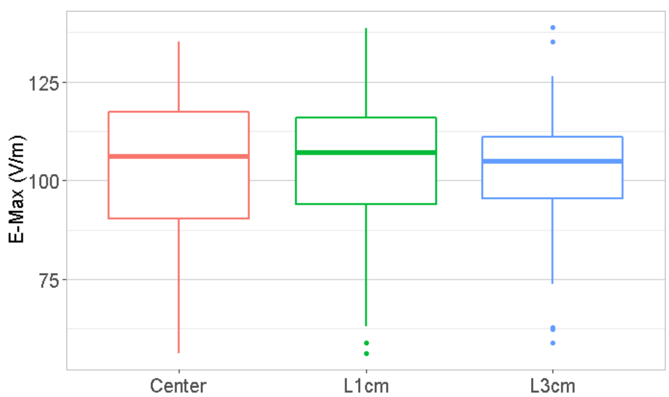

Fig. 6. Comparison of E-Max (V/m) between different positions of D-B80 coil

The boxplots in Fig. 6 did not show similar increasing trend of E-Max as in Fig. 4 for Figure-8 coil, but we noticed that the distance between 1st and 3rd quartiles decreased as the coil position changing from center to the left. In other words, when moving the coil from center to the left, the variation of E-Max becomes smaller, which means more data were located within a narrower range. For D-B80, anatomical variations play an less important role on E-Max in L3cm group than in Center and L1cm groups. It can be verified by the spread of data decribed by five number summaries in Table III that there is no trend of E-Max and the variation is smaller as the coil position changed from center to the left.

TABLE III
FIVE NUMBER SUMMARY OF E-MAX (V/M) FOR D-B80 COIL

	Minimum	1st Quartile	Median	3rd Quartile	Maximum
Center	56.24	90.32	106.10	117.33	135.14
L1cm	56.18	93.85	107.14	115.98	138.68
L3cm	58.95	95.31	104.84	110.94	138.88

Wilcoxon signed-rank test was conducted to test if there is a statistically significant difference of E-Max averaging across 50 head models between groups. P-values and 95% confidence intervals are reported in Table IV for each test. We can see from Table IV, the data provided enough evidence to show there is a significant difference between L1cm group and Center group on the average E-Max, while no significant differences detected from the other two pairs of comparison.

TABLE IV
TEST RESULTS OF DIFFERENCE BETWEEN POSITIONS FOR D-B80 COIL

D-B80 Coil	P-value	95% Confidence Interval
L1cm vs Center	0.0342*	(0.124, 2.955)
L3cm vs Center	0.7654	(-1.750, 3.319)
L3cm vs L1cm	0.3248	(-3.124, 1.122)

*statistically significant

Different from Figure-8 coil, when moving D-B80 coil from center to the left, there is barely significant change in maximum electric field intensity. For D-B80 coil, changing the position only changes the stimulated area on cerebellum without sufficiently altering the induced electric field. However, it reduced the significance of anatomical variations on the induced electric field by changing the coil position from center to the left.

In addition, V-half for each group were compared for D-B80 coil. The results are shown in Fig.7. Again different from Figure-8 coil, as changing the coil position from center to the left, V-Half showed a decreasing trend, which means the effectively stimulated volume in cerebellum became less and less.

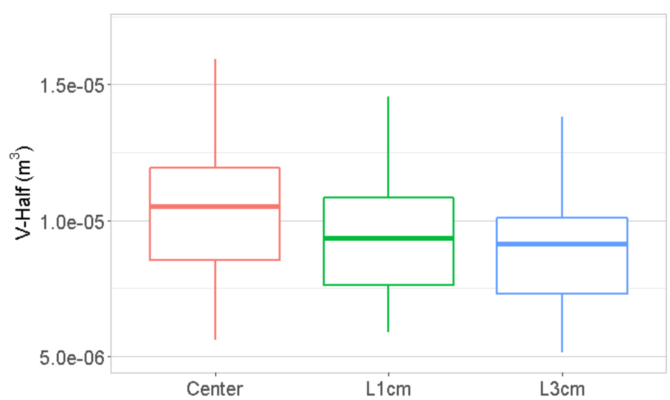

Fig. 7. Comparison of V-Half (m^3) between different positions of D-B80 coil

C. *Figure-8 vs D-B80*

Finally, the simulation results between Figure-8 coil and D-B80 coil at same position were compared. The boxplots of E-

Max and V-Half for both coils at each position are shown in Fig. 8 and Fig. 9. Also Wilcoxon signed-rank test results are given in Table V to figure out if there exists difference of E-Max between the two coils.

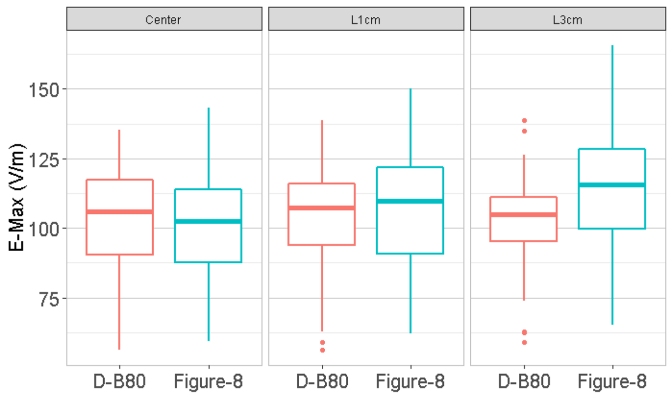

Fig. 8. Comparison of E-Max (V/m) between two coils at each position

It shows that there is no significant difference between Figure-8 coil and D-B80 coil at the center position. However, the average E-Max with Figure-8 coil is significantly greater than that with DB-80 coil at both 1cm and 3cm left to the center of cerebellum.

TABLE V
TEST RESULTS OF DIFFERENCE BETWEEN COILS AT EACH LOCATION

Figure-8 vs DB-80	P-value	95% Confidence Interval
Center	0.6157	(-3.142, 1.918)
L1cm	0.0006*	(1.830, 6.401)
L3cm	< 0.0001*	(8.516, 13.965)

The difference of V-half between Figure-8 and D-B80 coil at each position was shown in Fig. 9. As we can see, even though the V-Half values for D-B80 coil showed a decrease with position changing from center to the left, they are still obviously more than those for Figure-8 coil.

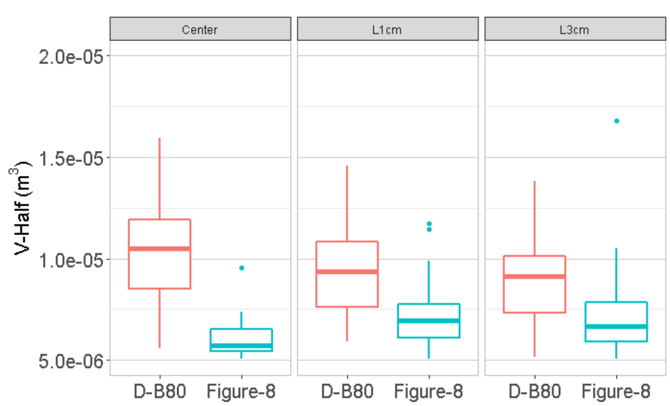

Fig. 9. Comparison of V-Half (m^3) between two coils at each position

IV. Conclusion

In this study, we have investigated the effects of coil geometry and anatomical variations on the strength and distribution of electric field in cerebellar TMS.

Figure-8 coil and D-B80 coil were positioned at three different locations and the induced stimulation profile was calculated for 50 MRI derived head models. The simulation results were compared between coils and between positions. Figure-8 coil and D-B80 coil have shown their difference on inducing electric field in cerebellum and to what extent the field strength was affected by coil position and anatomical variation.

As would be expected, we saw that the Figure-8 coil provided much more focal stimulation than the DB-80 coil.

Therefore, if the target is near the center of cerebellum, the performance of Figure-8 coil and D-B80 coil are similar. When the target is away from the center of cerebellum or under the circumstances that a focal target is needed, Figure-8 coil might be the better option to achieve higher electric field intensity and more focality. In addition, D-B80 coil might be used to stimulate deeper target area in cerebellum.

In TMS, common convention is to stimulate motor areas to determine the motor threshold, which is a metric that describes how much current needs to be going through a TMS coil for the subject to have an involuntary motor response. This motor threshold is then typically used to define dosing to other regions of the brain (in depression for example, stimulation is delivered to the dorsolateral prefrontal cortex at 120% the intensity of the motor threshold). For cerebellar TMS though, the position and the anatomy of the cerebellum is different than the motor cortex, therefore for all subjects, studies deliver stimulations at a specified stimulator output [3][4]. The current results can be used to assess the accuracy of using this type of dosing scheme to deliver stimulation.

Comparisons of the interquartile range show that stimulation is delivered at relatively similar intensity across the middle 50% of subjects, with the top receiving roughly 30% stronger stimulation intensities than the bottom for both coils (for the centered simulations). However, when the whole range of subjects is considered, this grows to roughly 140% for both coils. This variability is important for understanding the magnitude of stimulation effects and why there remains variability in how subjects respond to TMS.

Although the two coils produced nearly identical dosing variability at the center stimulation site, an interesting trend was observed in the DB-80 simulations, where the inter-quartile range for stimulation intensity dropped from 27.0 V/m in the center case, to 15.6 V/m in the L3cm case, suggesting that the L3cm has more consistent dosing across subjects.

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